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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,582	01/23/2002	Frederick R. Blattner	960296.95726	5379

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EXAMINER	
VOGEL, NANCY S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,582	BLATTNER ET AL.	
	Examiner	Art Unit	
	Nancy Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-30 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-30 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-7, drawn to a bacterium having a genome that is genetically engineered to be smaller than the genome of its native parent, classified in class 435, subclass 252.1.

II. Claims 8-16, drawn to a method for making a deletion in the genome of a bacterium at a selected genome region of known sequence, comprising introducing an artificial DNA sequence into the bacteria under conditions favoring homologous recombination, classified in class 435, subclass 478.

III. Claims 17-20, drawn to a method for making a deletion in the genome of a bacterium at a selected genome region of known sequence comprising providing a vector that comprises a tetracycline promoter, a lambda origin of replication controlled by the tetracycline promoter, and an antibiotic resistant gene, classified in class 435, subclass 477.

V. Claims 21-24, drawn to a method for replacing a selected region of a bacterial genome with a DNA sequence wherein the DNA sequence and the selected region can undergo homologous recombination, classified in class 435, subclass 477 and 478.

VI. Claims 25-27, drawn to a method for making a deletion in the genome a bacterium at a selected region of known sequence, comprising introducing

a vector comprising sequence-specific nuclease recognition site and two DNA sequences, classified in class 435, subclass 478.

VII. Claim 28-30, drawn to a method for replacing a selected region of a bacterial genome with a DNA sequence wherein the DNA sequence and the selected region can undergo homologous recombination, classified in class 435, subclass 477.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Group II and I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product as claimed can be made by another a materially different process, such as providing a vector that comprises a sequence-specific nuclease recognition site and two DNA sequences one of which is identical to a sequence that flanks a bacterial genome region to be deleted on one side and the other of which is identical to a sequence that flanks the bacterial genome region on the other side, wherein the two DNA sequences are located next to each other on the vector and wherein the sequence-specific nuclease recognition site is located outside the two DNA sequences on the vector; introducing the vector into the bacteria; introducing into the same bacteria an expression vector for a sequence-specific nuclease that recognizes the recognition site; introducing into the same bacteria a system that can increase the frequency of homologous recombination and at the same time expressing the

sequence-specific nuclease in the bacteria, and identifying bacteria in which the genome region to be deleted has been deleted.

Inventions of Group III and I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product as claimed can be made by another materially different process, such as providing a vector that comprises a sequence-specific nuclease recognition site and two DNA sequences one of which is identical to a sequence that flanks a bacterial genome region to be deleted on one side and the other of which is identical to a sequence that flanks the bacterial genome region on the other side, wherein the two DNA sequences are located next to each other on the vector and wherein the sequence-specific nuclease recognition site is located outside the two DNA sequences on the vector; introducing the vector into the bacteria; introducing into the same bacteria an expression vector for a sequence-specific nuclease that recognizes the recognition site; introducing into the same bacteria a system that can increase the frequency of homologous recombination and at the same time expressing the sequence-specific nuclease in the bacteria, and identifying bacteria in which the genome region to be deleted has been deleted.

Inventions of Group VI and I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2)

that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product as claimed can be made by a materially different process, such as by making an artificial DNA sequence, the artificial DNA sequence comprising: on one end a sequence number one identical to a genome sequence on the left flank of the genome region to be deleted, followed by a sequence number two identical to a genome sequence on the right flank of the genome region to be deleted; on the other end a sequence number three identical to a genome sequence within the genome region to be deleted; and a sequence-specific nuclease recognition site between the sequence numbers one and two on one end of the linear DNA molecule, and the sequence number three on the other end of the linear DNA molecule, the recognition site is not present in the genome of the bacteria,; introducing the artificial DNA sequence into the bacteria under conditions favoring homologous recombination between the first and third sequences and sequences in the genome of the bacteria; introducing into the bacterium whose genome contains the correct site insertion of the linear DNA molecule an expression vector for a sequence-specific nuclease that recognizes the recognition site; expressing the sequence-specific nuclease in the bacteria; and collecting the bacterium that survives.

The invention of Groups I, and Groups IV and VI, are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). In the instant case the different products of Groups I are not used in the methods of Groups V and VII.

Inventions of Groups II-VI are biologically and functionally different and distinct from each other and thus one does not render the other obvious. The methods of Groups II-VII comprise steps which are not required for or present in the methods of the other groups: making an artificial DNA sequence comprising on one end a sequence number one identical to a genome sequence on the left flank of the genome region to be deleted, followed by a sequence number two identical to a genome sequence on the right flank of the genome region to be deleted; on the other end a sequence number three identical to a genome sequence within the genome region to be deleted; and a sequence-specific nuclease recognition site between the sequence numbers one and two on one end of the linear DNA molecule, and the sequence number three on the other end of the linear DNA molecule, the recognition site is not present in the genome of the bacteria (Group II); providing a vector that comprises a tetracycline promoter, a lambda origin of replication controlled by the tetracycline promoter and an antibiotic resistance gene and inserting a DNA into the vector comprising two DNA sequences located next to each other wherein one DNA sequence is identical to a sequence that flanks a bacterial genome region to be deleted on one side and the other DNA sequence is identical to a sequence that flanks the bacterial genome region on the other side (Group III); inserting a DNA insert into a vector which comprises a tetracycline promoter, a lambda origin of replication controlled by the tetracycline promoter, and an antibiotic resistant gene, said DNA insert comprising a sequence for replacing a selected region of the bacterial genome (Group IV); providing a vector comprising a sequence-specific nuclease recognition site and two DNA sequences one of which is

identical to a sequence that flanks a bacterial genome region to be deleted on one side and the other of which is identical to a sequence that flanks the bacterial genome region on the other side wherein the two DNA sequences are located next to each other on the vector (Group V); and providing a vector that comprises a sequence-specific nuclease recognition site and the DNA sequence for replacing the selected region of the bacterial genome, wherein the sequence-specific nuclease recognition site is located outside the DNA sequence on the vector (Group VI). The end result of the methods are different: a bacterial containing a deletion of DNA (Groups II, III, V) and a bacteria containing a DNA replacement (Groups IV and VI). Thus, the operation, function and effects of these different methods are different and distinct from each other. Therefore, the inventions of these different, distinct groups are capable of supporting separate patents.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone

number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NTV

2/10/04

TERRY MCKELVEY
PRIMARY EXAMINER